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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,384	05/03/2001	Jari Hovinen	TUR-106	6081
7590	03/09/2004			
James C. Lydon Attorney at Law Suite 100 100 Daingerfield Road Alexandria, VA 22314			EXAMINER LEWIS, PATRICK T	
			ART UNIT 1623	PAPER NUMBER
DATE MAILED: 03/09/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/847,384

Applicant(s)

HOVINEN ET AL.

Examiner

Patrick T. Lewis

Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 14-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 14-31 is/are rejected.
- 7) ☒ Claim(s) 32 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☒ Interview Summary (PTO-413)
Paper No(s)/Mail Date. 03062004.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Applicant's Response dated November 26, 2003

1. In the Response filed November 26, 2003, claims 1-13 were canceled and claims 14-32 were added. Applicant presented arguments directed to the rejection of claims 1-10 under 35 U.S.C. 112, first paragraph for failing to comply with the written description requirement; the rejection of claims 1-10 under 35 U.S.C. 112, second paragraph; the rejection of claims 1-2, 4-5, and 9-10 under 35 U.S.C. 102(b) as being anticipated by Kwiatkowski et al. Nucleic Acids Research, 1994, Vol. 22, pages 2604-2611 (Kwiatkowski); the rejection of claims 1, 3, and 5 under 35 U.S.C. 102(b) as being anticipated by Sigmund et al. Nucleosides & Nucleotides, 1997, Vol. 16, pages 685-696 (Sigmund); and the rejection of claims 1-5 and 8-11 under 35 U.S.C. 103(a) as being unpatentable over Kwiatkowski et al. Nucleic Acids Research, 1994, Vol. 22, pages 2604-2611 (Kwiatkowski) in combination with Sigmund et al. Nucleosides & Nucleotides, 1997, Vol. 16, pages 685-696 (Sigmund) and Nardone et al. WO 99/64431 (Nardone).
2. Claims 14-32 are pending. An action on the merits of claims 14-32 is contained herein below.
3. The rejection of claims 1-10 under 35 U.S.C. 112, first paragraph, for failing to comply with the written description requirement has been rendered moot in view of applicant's amendment dated November 26, 2003.

4. The rejection of claims 1-10 under 35 U.S.C. 112, second paragraph, has been rendered moot in view of applicant's amendment dated November 26, 2003.
5. The rejection of claims 1-2, 4-5, and 9-10 under 35 U.S.C. 102(b) as being anticipated by Kwiatkowski et al. Nucleic Acids Research, 1994, Vol. 22, pages 2604-2611 (Kwiatkowski) has been rendered moot in view of applicant's amendment dated November 26, 2003.
6. The rejection of claims 1, 3, and 5 under 35 U.S.C. 102(b) as being anticipated by Sigmund et al. Nucleosides & Nucleotides, 1997, Vol. 16, pages 685-696 (Sigmund) has been rendered moot in view of applicant's amendment dated November 26, 2003.
7. The rejection of claims 1-5 and 8-11 under 35 U.S.C. 103(a) as being unpatentable over Kwiatkowski et al. Nucleic Acids Research, 1994, Vol. 22, pages 2604-2611 (Kwiatkowski) in combination with Sigmund et al. Nucleosides & Nucleotides, 1997, Vol. 16, pages 685-696 (Sigmund) and Nardone et al. WO 99/64431 (Nardone) has been rendered moot in view of applicant's amendment dated November 26, 2003.

Claim Objections

8. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 18-31 have been renumbered 19-32.

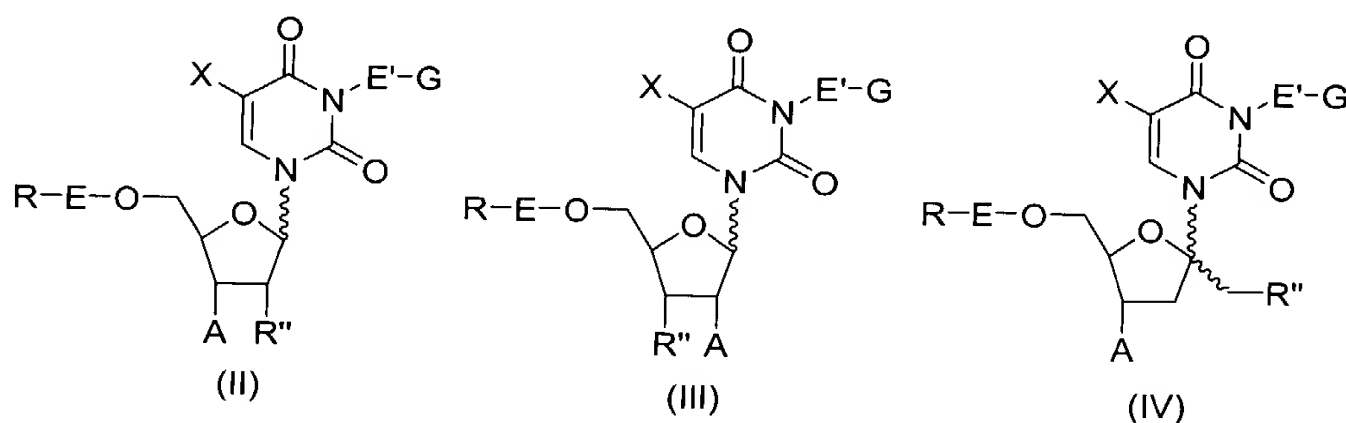
9. Claim 32 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

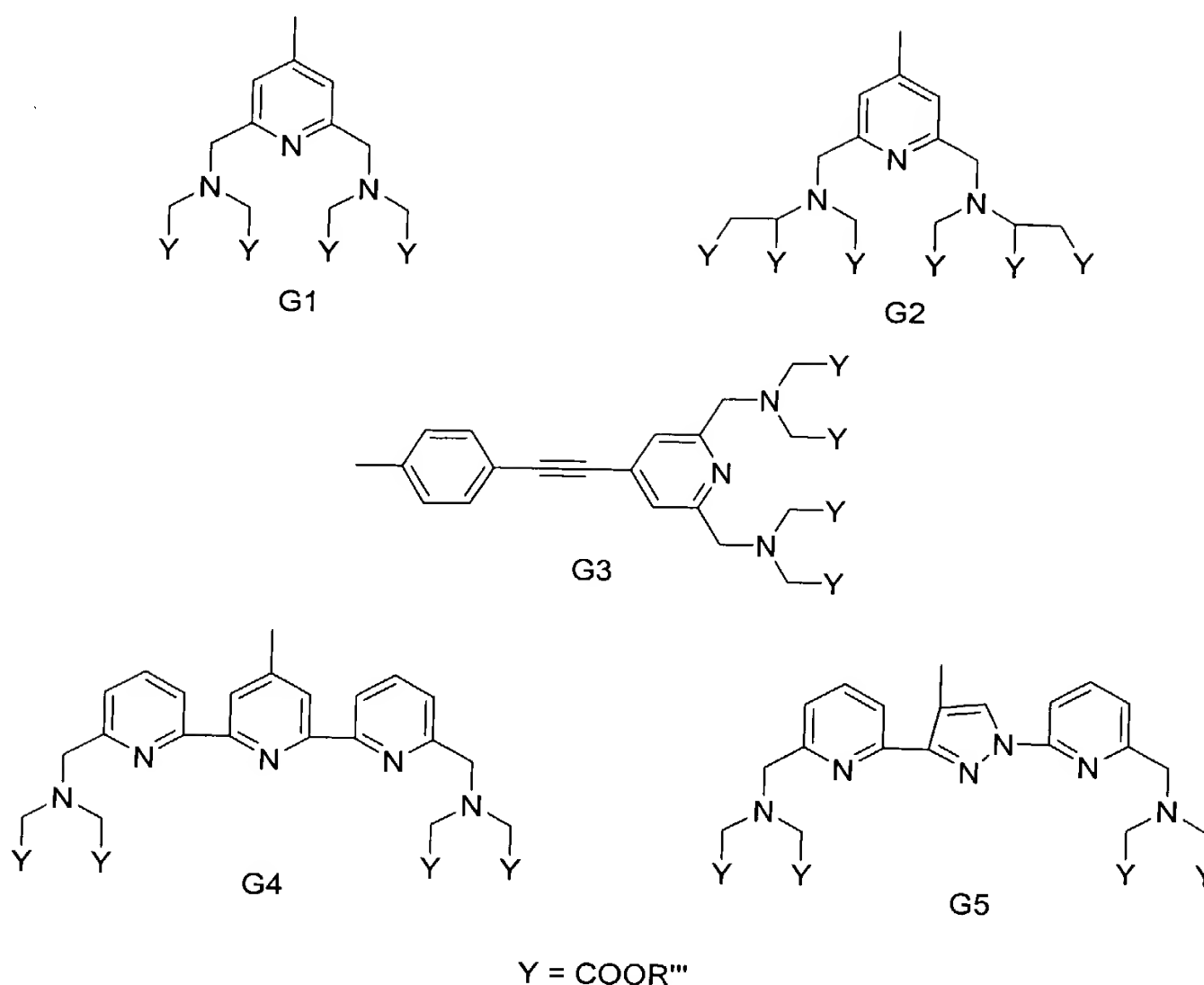
10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 14-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a labeling reactant of formulae (II), (III), and (IV)



wherein G is a moiety selected from the group consisting of G1, G2, G3, G4, or G5

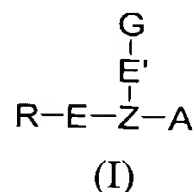


or wherein G is a protected functional group, wherein the functional group is amino, aminooxy, carboxyl, or thiol and wherein the protecting group is phthaloyl, trityl, 2-(4-nitrophenylsulfonyl)ethoxycarbonyl, fluorenylmethyloxycarbonyl, benzyloxycarbonyl or t-butoxycarbonyl for amino and aminooxy, alkyl for carbonyl, and alkyl or trityl for thiol, does not reasonably provide enablement for a labeling reactant of formula (I) wherein G is a moiety other than a moiety set forth supra. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

A disclosure in an application, to be complete, must contain such description and details as to enable any person skilled in the art or science to which it pertains to make

and use the invention as of its filing date, *In re Glass*, 181 USPQ 31; 492 F.2d 1228 (CCPA 1974).

The instant specification is drawn to a labeling reactant of formula (I),



suitable for labeling an oligonucleotide wherein R is a protecting group or not present; A is a phosphorylating moiety or a solid support tethered to Z via a linker arm; Z is a bridge point; E is a linker arm between R and Z; E' is a linker arm between G and Z; and G is a bivalent aromatic structure, tethered to two iminodiacetic acid ester groups; a chelate structure as shown in claim 1; or a protected functional group. While the prior art setting may be mentioned in general terms, the essential novelty, the essence of the invention, must be described in such details, including proportions and techniques where necessary, as to enable those persons skilled in the art to make and utilize the invention. A broad claim requires a correlatively broad and sufficient disclosure to support it. Presently, the examples in the instant specification are limited to the preparation of compounds 1-38, introduction of primary amino groups to the oligonucleotide structure with the aid of compound 3, introduction of lanthanide(III) chelates to the oligonucleotide structure with the aid of compound 8, and the introduction of a lanthanide(III) chelate to the oligonucleotide structure with the aid of compound 38. Examples and description should be of sufficient scope as to justify the scope of the claims. Where the constitution and formula of a chemical compound is stated only as a probability or speculation, the disclosure is not sufficient to support

claims identifying the compound by such composition or formula. A disclosure involving a new chemical compound or composition must teach persons skilled in the art how to make the compound. The process is considered to be incomplete wherein applicants set forth the preparation of compounds wherein various moieties are left undefined in full, clear and exact terms.

The instant specification invites the skilled artisan to experiment. The factors which must be considered in determining undue experimentation are set forth in *In re Wands*, 8 USPQ2d 1400. The factors include: 1) quantity of experimentation necessary, 2) the amount of guidance presented, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the predictability of the art, and 7) the breadth of the claims.

With regard to factors one, two, and three cited above, the quantity of experimentation needed to determine the specific chemical formula of the instantly claimed labeling reactant and the quantity of experimentation required to produce said labeling reactant would impose an undue burden upon the skilled artisan. There has not been provided adequate guidance in the written description for preparing labeling reactants commensurate in scope with applicant's claims. The examiner notes that the moiety G encompasses a broad and diverse set of chemical structures each of which having its own set of electronic, steric, solubility, and reactivity considerations. With the exception of the moieties set forth by the examiner supra as having support in the specification, applicant has failed to teach how the moieties represented by the variable G are attached to the chemical core via linker arm E'. It is also noted that linker arm E'

as claimed encompasses potentially millions of permutations—none of which attachments to the moiety G are taught. It is further noted that the linker arm may not be present.

With regard to factors four, five and six, it is noted that there is a great deal of unpredictability in the synthesis of organic compounds, especially those incorporating diverse, reactive functionalities. The specification provides no guidance which would lead one of ordinary skill in the art to select one point of attachment over another with respect to the moiety G. There are no teachings in the prior art which would predict points of attachment. Latva et al. *Journal of Luminescence* (1997), Vol. 75, pages 149-169 (Latva) is noted. Latva teaches several Lanthanide (III) chelates; however, Latva does not teach the specific attachments of the chelates to nucleoside or nucleotide cores directly or via a linker arm.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 14-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The terms “temporary protecting group” and “permanent protecting group” render claims in which they appear indefinite. Protecting groups are by nature “temporary”. In the absence of a chemical name or structural formula distinctly setting forth what moieties are embraced by said terms one of ordinary skill in the art would not be apprised of the metes and bounds of the instantly claimed compounds.

The phrase "can be substituted" renders claims in which it appears indefinite as it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d). Additionally, in the absence of distinct modifications to the chemical core claimed or distinct language to describe the structural modifications or the chemical names of substituted compounds of this invention, the identity of said substituted compounds would be difficult to describe and the metes and bounds of said substituted compounds applicant regards as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claims.

The phrase "one of the hydrogen atoms is substituted with E'" renders claims in which it appears indefinite as applicant has failed to distinctly set forth which hydrogen said phrase refers.

The term "TAMRA" has not been defined by the claims or specification rendering all claims in which said term appears indefinite.

Regarding claims 14, 29, and 30, applicant has failed to distinctly set forth how the structures represented by the variable G are attached to the linker E'. Said structures are seen to incorporate several potential points of attachments. The structures recited in claim 28 also incorporate dangling valences. In the absence chemical structures setting forth distinct points of attachments, all claims reading upon said structures represented by the variable G are indefinite.

Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between

the elements. See MPEP § 2172.01. The omitted elements are: the protected functional group. Also, claim 18 does not end in a period.

Regarding claims 23-27, recitations wherein the nucleotide sugar is ribose lacks antecedent basis.

Conclusion

14. Claims 14-32 are pending. Claims 14-31 are rejected. Claim 32 is objected to. No claims are allowed.

Contacts

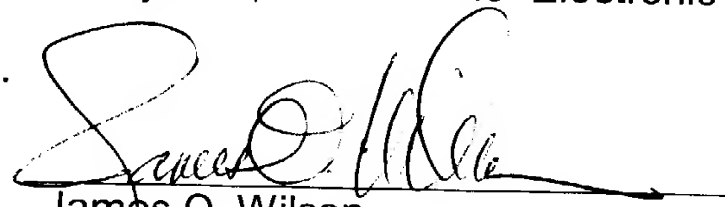
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on M-F 10:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patrick T. Lewis, PhD
Examiner
Art Unit 1623

ptl
March 6, 2004



James O. Wilson
Supervisory Patent Examiner
Technology Center 1600